

## Effect of individual viruses detected in ARI during Infancy on IPFT at 3-years of Age

### Rhinovirus (RV)

TBFVL indices for flow viz.  $t_{PTEF}/t_E$ ,  $TEF_{50}$ ,  $TEF_{25}$ ,  $TEF_{10}$ ,  $TEF_{50}/PTEF$ ,  $TEF_{25}/PTE$ ,  $TEF_{10}/PTEF$ , and  $V_{PTEF}/V_E$  were significantly increased in children with documented ARI with RV during infancy in comparison to children without any ARI episode. There was no significant difference in RTC indices in the two groups. In RVRTC, indices for forced volume viz.  $FEV_{0.5}$ ,  $FEV_{0.75}$ ,  $FEV_{1.0}$  and  $FEV$  and indices for forced flow rate viz.  $MEF_{10}$ ,  $MEF_{25}$  &  $FEF_{25-75}$  were significantly decreased in children at 3-years of age with documented rhinovirus ARI during infancy ([See Supplementary table 2](#)).

On multivariable analysis, decreased  $FEV_{1.0}$  at 3-years was significantly associated with detection of RV in ARI during infancy ( $p=0.009$ ) and lower weight at 3 years ( $p=0.003$ ). Presence of RV in ARI during infancy reduced the  $FEV_{1.0}$  by 20.8 mL (95% CI: -35.3, -5.3). Similar results were found in other RVRTC indices viz.  $FEV_{0.75}$  ( $\beta$  coefficient = -18.36, 95% CI: -31.36, -5.36,  $p=0.006$ ),  $FEV_{0.5}$  ( $\beta$  coefficient = -14.51, 95% CI: -24.76, -4.25,  $p=0.006$ ),  $FEF_{25-75}$  ( $\beta$  coefficient = -55.28, 95% CI: -89.2, -21.33,  $p=0.002$ ) and  $MEF_{25}$  ( $\beta$  coefficient = -63.25, 95% CI: -93.24, -28.26,  $p<0.001$ ).

### Respiratory Syncytial Virus (RSV)

$TEF_{50}/PTEF$  was the only TBFVL index, which was significantly increased in children at 3-year of age with documented RSV ARI during infancy. There was no significant difference in RTC indices. In RVRTC, the indices for forced expiratory volume viz.  $FEV_{0.5}$ ,  $FEV_{0.75}$  and  $FEV$  and for forced expiratory flow rate viz.  $MEF_{10}$ ,  $MEF_{25}$  &  $FEF_{25-75}$  were significantly decreased in children at 3-years of age with documented RSV infection during infancy ([See Supplementary table 2](#)).

FEV<sub>1.0</sub> ( $\beta$ coefficient = -30.04, 95% CI: -30.88, -6.25,  $p=0.004$ ), FEV<sub>0.75</sub> ( $\beta$ coefficient = -25.06, 95% CI: -39.93, -10.19,  $p=0.001$ ), FEV<sub>0.5</sub> ( $\beta$ coefficient = -18.57, 95% CI: -30.89, -6.25,  $p=0.004$ ), FEF<sub>25-75</sub> ( $\beta$ coefficient = -62.47, 95% CI: -104.47, -20.46,  $p=0.004$ ), MEF<sub>10</sub> ( $\beta$ coefficient = -72.2, 95% CI: -111.69, -32.7,  $p<0.001$ ) and MEF<sub>25</sub> ( $\beta$ coefficient = -65.19, 95% CI: -109.6, -20.78,  $p=0.004$ ) were decreased significantly with the occurrence of RSV ARI during infancy after adjusting for other factors including tidal volume at birth.

### Human Corona Virus (HCoV)

In TBFVL, there was a significant increase in TEF<sub>25</sub>, TEF<sub>10</sub>, and TEF<sub>25</sub>/PTEFT in children with documented HCoV ARI during infancy compared to children who did not have any documented ARI episodes. There was no significant difference in RTC indices. In RVRTC, indices for forced timed volume viz. FEV<sub>0.75</sub>, FEV<sub>0.5</sub> and for forced flow rate viz. FEF<sub>25-75</sub>, MEF<sub>25</sub>, MEF<sub>10</sub>, and PEF was significantly decreased in children with HCoV ARI during infancy ([See Supplementary table 2](#)).

On multivariate analysis, MEF<sub>25</sub> ( $\beta$ coefficient = -63.80, 95% CI: -111.79, -15.81,  $p=0.01$ ), FEF<sub>25-75</sub> ( $\beta$ coefficient = -62.19, 95% CI: -108.74, -15.66,  $p=0.009$ ), FEV<sub>0.5</sub> ( $\beta$ coefficient = -15.74, 95% CI: -29.85, -1.63,  $p=0.03$ ) and PEF ( $\beta$ coefficient = -56.87, 95% CI: -106.58, -7.17,  $p=0.02$ ) were significantly decreased in children with ARI with HCoV in infancy as compared to those who had no ARI in infancy.

### Human Metapneumovirus (HMPV)

TBFVL indices for flow rate TEF<sub>10</sub>, TEF<sub>25</sub>, TEF<sub>50</sub>, and flow ratio TEF<sub>25</sub>/PTEF were significantly increased in children with documented HMPV ARI during infancy compared with children who did not have documented ARI episode. In RTC,  $V'_{\max, \text{FRC}}$  was also considerably increased in

children with HMPV infection. RVRTC indices for forced flow rate viz. FEF<sub>25-75</sub>, MEF<sub>25</sub>, and MEF<sub>10</sub> were significantly decreased in children with HMPV infection ([See Supplementary table 2](#)).

On multivariate analysis, MEF<sub>25</sub> ( $\beta$  coefficient = -73.29, 95% CI: -17.99, -128.59,  $p=0.01$ ), MEF<sub>10</sub> ( $\beta$  coefficient = -74.37, 95% CI: -22.54, -126.19,  $p=0.006$ ), and FEF<sub>25-75</sub> ( $\beta$  coefficient = -61.59, 95% CI: -9.43, -113.74,  $p=0.02$ ) were significantly decreased in children with ARI with HMPV in infancy. TEF<sub>25</sub>/PTEF ( $\beta$  coefficient = 4.72, 95% CI: 0.34, 9.11,  $p=0.03$ ) and  $V'_{\max, \text{FRC}}$  ( $\beta$  coefficient = 44.71, 95% CI: 10.83, 78.58,  $p=0.01$ ) were higher in children with HMPV ARI in infancy as compared to those who had no ARI in infancy.  $V'_{\max, \text{FRC}}$  was also associated with the weight and height at 3 years of age.